REMARKS

Claims 34-36 and 46-66 are pending in this application. Claims 36, 49, 52, and 60 are amended for clarity. Therefore, no new matter is introduced. The Office Action are discussed below.

Claim Rejections under 35 USC § 112:

New matter rejection:

On pages 2-3 of the Office Action, the examiner rejects claims 49, 52 and 60 allegedly for failing to comply with written description requirement and asserts a new matter rejection. According to the examiner, the specification discloses only the growth medium comprising both yeast and soy hydrolysate and not the claimed method in which only one of the hydrolysates selected from soy or yeast hydrolysate are utilized. Applicants respectfully disagree with the examiner and refer that the specification also discloses medium in which only one of the hydrolysates selected from soy or yeast hydrolysate are utilized. For example, paragraph [58] that describes "The results demonstrate that yeast and soy hydrolysate alone supported cell growth" and "....supplementation of the basal medium with a combination of soy hydrolysate and yeast hydrolysate the final cell density reached was significantly increased compared to a medium comprising solely soy or yeast hydrolysate." Clearly, the specification provides examples of medium in which only one of the hydrolysates selected from soy or yeast hydrolysate are utilized.

However, without acquiescing in the rejection and in the interest of advancing the prosecution, applicants amend claims 49, 52, and 60 for clarity to recite "an animal protein free culture medium comprises a soy and a yeast hydrolysate...." Withdrawal of the new matter rejection is therefore solicited.

Enablement Rejection:

On pages 3-6 of the Office Action, the examiner rejects claims 34-36 and 46-66 allegedly for failing to comply with the enablement requirement. Applicants respectfully

disagree with the examiner and submit that the examples as disclosed in the specification provide sufficient support and meet the enablement requirement.

The examiner relied on the Shubiya's (US 6,406,909) failure to achieve cell growth for the level of unpredictability in the art and opined that "it cannot be predicted whether any particular type of culture media, will successfully support the growth of any cell type as claimed by applicant." Applicants point out that the examiner did not understand why Shubiya failed to grow certain cells. As clarified in the responses to previous Office Actions (see responses filed on April 22, 2008 and August 7, 2007), Shibuya did not use the same medium as recited in the claimed invention. For example, Shibuya medium does not exclude "Insulin Human Recombinant" (see Shibuya col. 5, lines 8-10, and 23-27). Shibuya's "serum-free medium" by definition includes the basal medium composition (see for example, Shibuya Table 1), which includes "various peptide hormones and growth factor proteins that are not directly separated from animals, i.e., includes animal proteins that are produced with recombinant techniques,...." (see Shibuya col. 5, lines 23-27). Therefore, by definition, the instantly claimed "serum-free medium" does not encompass recombinantly-produced animal proteins. The claimed methods avoid animal proteins, whereas the medium disclosed by Shibuya employs animal proteins. Thus, the examiner's citation of Shubiya is not relevant, and is insufficient for establishing unpredictability of the claimed method of producing an immunogenic composition using the medium recited in the instant claims.

Applicants also submit that the specification provides several working examples (see Examples 1 to 4, at paragraphs [53] to [70], for example), in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is evident from the above clarifications that the specification discloses and provides guidance to one skilled in the art for producing an immunogenic composition utilizing the "animal protein free" medium as recited in the claims. In this context applicants refer the examiner to dictates of the MPEP that:

"Any analysis of whether a particular claim is supported by the

> disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde,* 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)."
>
> *See* MPEP §2164.01 (Rev. 6, September 2007 at 2100-193).

Applicants further submit that an undue experimentation would not be required to practice the claimed invention in light of the methods described in the specification and based on what is known in the art. Regarding the examiner's concern of the lack of guidance and working examples, applicants refer to the fact that the:

> "...experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).
>
> *See* MPEP §2164.01 (Rev. 6, September 2007 at 2100-194).

Applicants refer that working examples are not required in a patent application, and the mere absence of such examples is not sufficient to support a written description rejection. *Falkner v. Inglis*, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). Nevertheless, the specification provides working examples (see Examples 1-4), which describe methods of viral propagation and cultivation using media according to invention.

Applicants, in this context, refer the examiner to the MPEP that:

> "...A single working example in the specification for a claimed invention is enough to preclude a rejection which states that nothing is enabled since at least that embodiment would be enabled. However, a rejection stating that enablement is limited to a particular scope may be appropriate.

> The presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims."
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> *See* MPEP §2164.02 (Rev. 6, September 2007 at 2100-196).

Accordingly, withdrawal of the enablement rejection is solicited.

Claim Rejection under 35 USC § 103:

On pages 6-10 of the office action, the examiner has maintained the obviousness rejection of claims 34-36 and 46-66 over Price *et al.* (WO 98/15614) in view of Kistner *et al.* (US Patent 5,753,489), Luderer *et al.* (US P patent 4,282,315), Gauri *et al.* (US Patent 4,322,404) and Quest International Product Information, Norwich NY, 1995, and Sheffield Pharma Ingredients, Cell Nutrition, Hydrolyzed Proteins & Yeast Extracts, Technical Manual). Applicants respectfully disagree with the examiner and refer to the arguments as submitted on April 22, 2008.

The examiner has previously asserted (see Office Action of January 28, 2008) that Price *et al.* on pages 4-5 disclose that the plant extracts, including soy and yeast hydrolysates, are useful for replacing all components of animals in culture medium. The examiner referred to page 22 of Price *et al.* that discloses "the present invention also relates to methods for replacing or substituting animal-derived products with plant peptides, plant lipids, plant fatty acids, and/or enzymatic digests or extracts of yeast cells (or combinations thereof). Such plant and/or yeast-derived nutrients may be substituted for any number of animal-derived culture medium components or substituents...." Thus, the examiner alleges that the reference teaches the wholesale replacement of animal products in culture media by the disclosed plant and yeast hydrolysates.

On page 10 of the current Office Action, the examiner also asserts that the wording of the Price *et al.* reference, in which it is stated that "the present invention also relates to methods for replacing or substituting animal-derived products with plant

peptides, plant lipids, plant fatty acids, and/or enzymatic digests or extracts of yeast cells (or combinations thereof)" is not particularly relevant. The examiner believes that a "substitution" for animal products would result a culture medium in which animal products are not used. Applicants again disagree with the examiner and point out that Price *et al.* reference does not disclose an "animal protein free medium" as the examiner is trying to reconstruct the reference by substituting the animal products.

Applicants submit that a conclusion to the contrary can only be attained through a proscribed hindsight reconstruction of the prior art in view of the teachings of the applicants' specification. *See Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 907, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988). In this case, the claimed methods require that an "animal protein free" medium be used and not replacing or substituting certain animal-derived products, as the examiner is attempting to do by reconstructing the Price *et al.* reference based on the knowledge gleaned from the instant specification. Such reconstruction is impermissible.

An inquiry that focuses on substitutions and differences, instead of the invention as a whole, is legally improper. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 93 (Fed. Cir. 1986). Also, focusing on the obviousness of substitutions and differences instead of on the invention as a whole is legally improper way to simplify the difficult determination of obviousness. *See Hodosh v. Block Drug Co.*, 786 F.2d 1136, 229 USPQ 182 (Fed. Cir. 1986).

In addition, applicants reiterate that the cited references do not motivate one skilled in the art to use an "animal protein free" medium in combination with the other cited references to arrive at the claimed invention that utilizes an "animal protein free" medium in a method of producing an immunogenic composition. Applicants also emphasize that by definition, unlike the media disclosed in the cited references, the animal protein free medium recited in the claims does not encompass recombinantly-produced animal proteins. Therefore, any combination of the cited references would not result in a method of producing an immunogenic composition utilizing an "animal protein free medium" as recited in the claims.

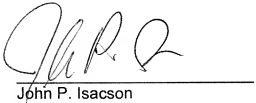
In view of the above, applicants submit that a *prima facie* case of obviousness

has not been established by the examiner. Accordingly, withdrawal of the obviousness rejection is earnestly requested.

REQUEST

Applicants submit that claims 34-36 and 46-66 are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



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Date

John P. Isacson
Reg. No. 33,715

PROSKAUER ROSE LLP
1001 Pennsylvania Avenue, N.W.
Suite 400 South
Washington, D.C. 20004
Phone: 202-416-6800
Fax: 202-416-6899
Customer No. 61263